

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property
Organization
International Bureau



(43) International Publication Date
10 June 2004 (10.06.2004)

PCT

(10) International Publication Number
WO 2004/048408 A2

(51) International Patent Classification⁷: C07K 14/46 (74) Agent: VAN WESTENBRUGGE, ANDRIES et al.; Nederlandsch Octrooibureau, Scheveningseweg 82, P.O. Box 29720, NL-2502 LS The Hague (NL).

(21) International Application Number: PCT/NL2003/000831 (81) Designated States (national): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(22) International Filing Date: 25 November 2003 (25.11.2003) (84) Designated States (regional): ARIPO patent (BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

(25) Filing Language: English (30) Priority Data: 02079903.7 25 November 2002 (25.11.2002) NL

(71) Applicant (for all designated States except US): ACADEMISCH ZIEKENHUIS BIJ DE UNIVERSITEIT VAN AMSTERDAM [NL/NL]; Meibergdreef 9, NL-1105 AZ Amsterdam-Zuiddreef (NL).

(72) Inventors; and (75) Inventors/Applicants (for US only): PEPPELEN-BOSCH, Maikel, Petrus [NL/NL]; Obrechtstraat 74, NL-3572 EH Utrecht (NL). ZIVKOVIC, Danica [NL/NL]; Ramstraat 39, NL-3581 HE Utrecht (NL). DIKS, Sander [NL/NL]; Smalle haven 57, NL-5211 TJ 'S-Hertogenbosch (NL). BINK, Robert, Jozef [NL/NL]; Louis Armstrongkade 176, NL-2551 WV 'S-Gravenhage (NL).

Published:

— without international search report and to be republished upon receipt of that report

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

WO 2004/048408 A2

(54) Title: ASB TRANSCRIPTION REPRESSOR PROTEINS AND NUCLEIC ACIDS AND THEIR APPLICATION IN EXPANSION OF STEM CELLS

(57) **Abstract:** The present invention relates to methods for expansion of stem or progenitor cells. These methods rely on Asb-a polypeptides or nucleic acids to temporarily suppress differentiation of the cells, thus allowing proliferation and self-renewal of the stem or progenitor cells. Asb-a polypeptides and coding sequences define a class of polypeptides and nucleic acids that are both structurally and functionally highly conserved among vertebrates. Asb-a polypeptides contain 6 ankyrin repeats and a SOCS box that mediate the effect of the polypeptide on the regulation of specific subsets of genes involved in differentiation. The invention discloses various methods to increase the intracellular concentration of an Asb-a polypeptide for suppression of terminal differentiation of the stem or progenitor cells. The invention further relates to Asb-a polypeptides and nucleic acids, vectors and host cells for use in methods for their production and for use in the method for expansion of stem or progenitor cells, as well as to stem or progenitor cells containing exogenous Asb-a polypeptides and nucleic acids.